SHORT COMMUNICATION

Association of retinopathy and intima media thickness of common carotid artery in type 2 diabetic patients

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Background: This study was carried out in order to evaluate the relationship between retinopathy and carotid intima-media thickness (CIMT). **Materials and Methods:** In a cross-sectional study, 154 diabetic patients who had a history of diabetic disease were evaluated in two equal groups of 77 patients with and without retinopathy, respectively. CIMT was evaluated in all of the patients. **Results:** Mean age of the patients was 59.65 ± 9.37 years. Mean CIMT of all patients was 0.84 ± 0.18. CIMT of patients with retinopathy was significantly greater than patients without retinopathy ($P < 0.001$). CIMT also correlated with age, duration of diabetes, systolic blood pressure, blood urea nitrogen, and serum creatinine. **Conclusion:** CIMT may be used as a simple, available and noninvasive method for screening of macro and microvascular complication of diabetic patients.

Key words: Common carotid artery, diabetic retinopathy, intima-media thickness, sonography

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INTRODUCTION

Diabetes mellitus is the most common cause of end-stage renal disease, non-traumatic lower-limb amputation and blindness. Furthermore, diabetic retinopathy (DR) is the most important cause of visual loss worldwide. The prevalence of DR increases with duration of diabetes. Some other risk factors of DR development include poor glycemic control, type of diabetes, and the presence of associated disorders such as dyslipidemia, hypertension, smoking, pregnancy, and nephropathy.[1,2] DR could present as non-proliferative retinopathy, proliferative retinopathy or macular edema, however, the most important cause of visual loss among these patients is macular edema.[3,4] Retinopathy is essential for the diagnosis of diabetic nephropathy, but it presents in 90% and 60% of type 1 and 2 diabetic patients, respectively.[5] Because the rate of progression of retinopathy may be rapid, and treatment can be beneficial for reduction of disease progression, it is important to screen diabetic patients regularly for the development of retinopathy, so in type 1 diabetes, after 5 years and in type 2 diabetes, at the time of diagnosis and then annually, retinopathy should be evaluated.[6,7] One of the other complications of diabetes is generalized atherosclerosis which can be presented as ischemic heart disease, cerebrovascular accident or peripheral vascular disease. Diabetic atherosclerosis can be detected by measurement of intima-media thickness (IMT) of common or internal carotid artery (CIMT). The CIMT was used to predict of cardiovascular outcomes in diabetic patients.[8] The easy applicability and the noninvasive nature of B-mode ultrasonography make it suitable for using as a surrogate endpoint for measuring the atherosclerotic burden in people with cardiovascular risk factors.[9] The mean CIMT values by the different incidences were reported as 1.26 ± 0.6 mm (transversal), 1.17 ± 0.54 mm (longitudinal anterolateral), and 1.18 ± 0.58 mm (longitudinal posterolateral).[10] Increases in the thickness of the carotid IMT may be associated with an increased risk of myocardial infarction and stroke in old patients without a history of cardiovascular disease.[11] Mean CIMT was reported a reliable marker of risk of ischemic stroke in type 2 diabetic patients and could be used as a simple noninvasive screening test for the assessment of atherosclerosis in these patients.[12] Mean CIMT may be associated with age, systolic blood pressure (SBP), smoking, the ratio of low-density lipoprotein to high-density lipoprotein cholesterol, mean glycosylated hemoglobin value (HbA1c), and urinary albumin excretion rate.[13] In type 2 diabetic patients, significant predictors of IMT progression included albuminuria, advanced

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age, male sex, smoking, and higher SBP.[14] In diabetic patients without a history of clinical CVD, the presence of advanced stage of DR is associated with subclinical coronary artery disease.[15,16] DR was shown as subclinical atherosclerosis marker, so retinopathy may warrant a more careful cardiovascular assessment even in the early stages of diabetes.[17]

Intima-media thickness is a sensitive marker of early carotid atherosclerosis, so ultrasound CIMT measurement can be used to assess the cardiovascular risk and to determine indications for intensified diabetic treatment; on the other hand, DR is an early and reliable marker of microvascular disease, and probably diabetic nephropathy,[18] so the aim of our study was evaluation of relationship between retinopathy and CIMT as two valuable noninvasive methods for early detection of micro and macrovascular complication of diabetes.

MATERIALS AND METHODS

In a cross-sectional study (2012), 154 diabetic patients who had a medical history and follow-up in Imam Ali Clinic of Shahrekord were enrolled in the study. They were divided into two equal groups of 77 patients that were case group (with retinopathy) and control group (without retinopathy). Diabetes is defined as fasting blood sugar equal or more than 126 mg/dl.[19] DR is defined as a microvascular complication of diabetes that affect retinal arterioles and it has two forms as nonproliferative and proliferative retinopathy.[20] Exclusion criteria were: Age lesser than 40, presence of cataract in the ophthalmologic exam that prevents retinopathy evaluation, noncooperative patients during the study. It has been explained to the participants that all information will be confidential and a written consent form were filled in by all patients. Common carotid intima-media thickness (CIMT) is defined as the largest distance between the luminal intima interface and the medial adventitia interface that is located at 1 cm of the initiation of the common carotid artery[21] that was measured by one sonographist in recombinant position and using Doppler sonography devices (Siemens, G50, Germany). Demographic criteria such as age, duration of diabetes, body mass index (BMI), SBP and diastolic blood pressure (DBP), and laboratory results including fasting blood sugar (FBS), Glycated hemoglobin (HbA1c), blood urea nitrogen (BUN), and creatinine (Cr) were checked. BMI was measured by formula (body weight [Kg]/Length [m^2]) and laboratory tests were conducted by Biotecnica Instruments (BT 3000). Collected data were entered to SPSS (Statistical Package for the Social Sciences, version 19.0, SPSS Inc, Chicago, Ill, USA) and analysis was done by *t*-test, Chi-square test, and Pearson correlation. This study was the result of research project number of 986, which approved by the research committee of Shahrekord University of Medical Sciences. Data are presented as mean (standard deviation).

RESULTS

Mean age of the patients was 59.65 ± 9.37 years. Mean age of the patients with retinopathy (Group 1) was 62.5 ± 9.75 years and in the patients without retinopathy (Group 2) was 58 ± 10 years (P = 0.006). Mean CIMT of all patients was 0.84 ± 0.18 and in the female and male patients were 0.82 ± 0.16 mm and 0.88 ± 0.22 mm respectively (P = 0.03). In all of the patients, CIMT was associated with age, duration of diabetes (based on history), SBP, serum BUN, and Cr [Table 1]. The number of male and female in Group 1 was 34 (44.2%) and 43 (55.8%) and in Group 2 were 21 (27.3%) and 56 (72.7%), respectively. CIMT of the patients of Group 1 was significantly greater than Group 2 (P < 0.001). Mean HbA1c in Group 1 ad 2 were 7.20 ± 1.21 and7.04 ± 1.33, respectively (P = 0.39). Table 2 showed that in patients of Group 1, CIMT was correlated only with SBP (P = 0.01); however in the

Table 1: Comparison of different variables in two groups of the patients

Variables	Age (years)	BMI (kg/m²)	SBP (mmHg)	DBP (mmHg)	BUN (mg/dL)	Cr (mg/dL)	HbA1c (%)	CIMT (mm)
Group 1	62.01±9.08	28.94±4.73	143.37±20.04	83.11±11.5	26.31±12.79	1.45±0.75	7.39±1.19	0.95±0.18
Group 2	57.29±9.84	29.63±4.07	134.94±19.03	84.35±15.6	21.13±8.79	1.1±0.36	7.01±1.29	0.73±0.11
P	0.002	0.33	0.008	0.57	0.004	<0.0001	0.39	0.0001

Group 1 = Diabetic patients with retinopathy; Group 2 = Diabetic patients without retinopathy. BMI = Body mass index; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; BUN = Blood urea nitrogen; Cr = Creatinine; CIMT = Carotid intima-media thickness; HbA1c = Glycosylated hemoglobin

Table 2: Association of CIMT with different variables in the patients

Variable	Age	BMI	SBP	DBP	BUN	Cr	HbA1c	FBS
Patients with retinopathy								
Correlation coefficient	0.14	0.003	0.276	0.179	0.016	0.067	0.069	0.183
P	0.2	0.981	0.01	0.12	0.89	0.56	0.55	0.11
Patients without retinopathy								
Correlation coefficient	0.256	0.179	0.186	0.274	0.19	0.008	0.09	0.07
P	0.2	0.11	0.11	0.03	0.09	0.94	0.42	0.51

BMI = Body mass index; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; BUN = Blood urea nitrogen; Cr = Creatinine; CIMT = Carotid intima-media thickness; HbA1c = Glycosylated hemoglobin; FBS = Fasting blood sugar

patients of Group 2, CIMT was correlated with DBP. To remove confounding bias effect, linear regression model was used and the correlation between DR and CIMT was illustrated.

DISCUSSION

We found a significant association between CIMT and retinopathy in type two diabetic patients. Prevalence of DR in type 2 diabetic patients was reported 34.6% in Yau *et al*. study with no difference in male and female,[22] whereas Zhang *et al*. showed slightly more common in male patients.[2] Besides, Harris *et al*. found a greater prevalence and severity of DR in non-hispanic and Mexican Americans with type 2 diabetes.[23] There are a few studies about correlation of CIMT and retinopathy in diabetic patients, for example, Miyamoto in evaluation of 102 diabetic patients showed the significant correlation between retinopathy and common carotid artery thickness,[24] also Torres *et al*. in a study on 173 patients with hypertension showed, significant and independent association of carotid intima-media thickness with arteriolar caliber of retina.[25] In our study CIMT was associated with age, duration of diabetes, SBP, serum BUN, and Cr whereas Cardoso *et al*. found the correlation of CIMT with age, male sex, smoking status, and ambulatory blood pressure.[26] Ogawa *et al*. in a study on 634 type 2 diabetic patients reported the positive correlation of CIMT and patients BMI, also he found correlation between maximum BMI and retinopathy, but we didn't find this association in the patients. The reason of this discrepancy may be due to different number of patients in two studies.[27] Correlation of CIMT and HTN was reported in some studies,[12,26] also in our study CIMT was correlated with SBP in patients with retinopathy and with DBP in patients without retinopathy, however, Alizadeh *et al*. in a study on 40 diabetic patients did not find these correlation.[28] Similar to our results, in Ogawa *et al*. study also CIMT had not correlation with control of blood sugar.[29] About association of HbA1c and CIMT we did not find a significant correlation. Furthermore similar result was found by Choi *et al*. in the study on 370 type 2 diabetic patients.[30]

Small sample size is a limitation in our study, so we suggest more studies to be carried out using larger sample size. Therefore, the relationship between CIMT and other complications of diabetes such as microalbuminuria, macroalbuminuria or neuropathy need to be evaluated.

CONCLUSION

In diabetic patients, CIMT is a marker of atherosclerosis and macrovascular damage which has had a correlation with DR (as a potential reliable marker of microvascular damage), so we may use sonographic measurement of CIMT as a simple, available, and noninvasive method for screening of macro and microvascular complications among diabetic patients.

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AUTHOR'S CONTRIBUTION

All authors have contributed in designing and conducting the study. All authors have assisted in preparation of the first draft of the manuscript or revising it critically for important intellectual content. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

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